Methods

Retrospective review of medical records were undertaken in the participating tertiary hospitals (n=5) to identify children (≤ 18 years) with refractory steroid resistant nephrotic syndrome (SRNS) who received rituximab infusion between March 2012 to January 2018. Objective was to assess effectiveness of rituximab among children with refractory SRNS. Primary outcome was assessed by number of children achieving either complete (CR) or partial remission (PR), as even PR has been shown to improve renal survival [1].

NS and SRNS were defined as per Kidney Disease Improving Global Outcomes (KDIGO) [2]. Primary SRNS were non-responder to initial dose of steroid and those who developed steroid resistance after initial response were secondary SRNS. Refractory SRNS was defined as failure to achieve remission even after minimum 6 months of CNI exposure with acceptable trough levels (Cyclosporine 80- 120 ng/ml and tacrolimus 4 – 8 ng/ml) [2, 3].

Rituximab was given at 375 mg/m^2 per infusion and each cycle was defined as paired infusion given within a span of two weeks. Follow up was until either last clinic visit or change of immunosuppressant or repetition of rituximab. CR was defined as urine protein to creatinine ratio (Up/Uc) <0.2 mg/mg. PR defined as Up/Uc between 0.2 and 2 mg/mg OR serum albumin >2.5 g/dL. No response (NR) as Up/Uc >2 mg/mg AND serum albumin <2.5 g/dL [4].

Statistical analysis

SigmaPlot software (version 13) was used for the statistical analysis. Continuous variables were expressed as median with inter-quantile range. Mann-Whitney U-test was used to compare continuous variables between two groups and chi-square test to compare proportions.The Kaplan–Meier method was performed to calculate response to rituximab and censored at last follow up or if a further rituximab dose was given. All P values were two-tailed, and values < 0.05 were considered statistically significant.

Ethical approval was obtained.

References for methods section:

1. Mekahli D, Liutkus A, Ranchin B, Yu A, Bessenay L, Girardin E et al. Long-term outcome of idiopathic steroid-resistant nephrotic syndrome: a multicenter study. Pediatr Nephrol. 2009 Aug;24(8):1525-32.
2. Kidney Disease Improving Global Outcome (KDIGO) (2012). Steroid resistant nephrotic syndrome in children. Kidney Int Suppl 2:172-176
3. Trautmann A, Vivarelli M, Samuel S, Gipson D, Sinha A, Schaefer F et al. IPNA clinical practice recommendations for the diagnosis and management of children with steroid-resistant nephrotic syndrome. Pediatr Nephrol. 2020 May 7. Online ahead of print.
4. Jellouli M, Charfi R, Maalej B, Mahfoud A, Trabelsi S, Gargah T. Rituximab in The Management of Pediatric Steroid-Resistant Nephrotic Syndrome: A Systematic Review. J Pediatr. 2018 Jun; 197:191-197.e1.